Claims

1. An artificial peptide or polypeptide comprising a conformationally discriminating epitope (CDE) in its native conformation, wherein the CDE is structurally stabilized by circularization.

2. The peptide or polypeptide claim 1, wherein it comprises artificial or/and glycosylated amino acids.

3. The peptide or polypeptide claim 1 or 2, wherein it is conjugated to a carrier molecule.

4. The peptide or polypeptide of any one of the preceding claims, wherein it comprises a CDE of an Fc receptor.

5. The peptide or polypeptide of claim 4, wherein it comprises a CDE of FcγRIIb or FcγRIIa, the CDE comprising at least residue which is unique to either FcγRIIb or FcγRIIa.

6. The peptide or polypeptide of claim 5, wherein the CDE comprises amino acids 27 to 30, and/or amino acids 127 to 135, and/or 160 to 171 of FcγRIIb according to SEQ ID NO: 2 or the corresponding amino acids of FcγRIIa according to SEQ ID NO: 1, or the amino acid sequence according to SEQ ID NO: 3.

7. The peptide or polypeptide of any one of claims 4 to 6, wherein it is conjugated to FcγRIIb or FcγRIIa.

8. A method of producing a peptide carrying a conformationally discriminating epitope (CDE) for the generation of antibodies specifically recognizing a protein of interest carrying such an epitope,

wherein the method comprises:

(a) providing a protein of interest,

(b) identifying a CDE on that protein,

(c) producing a peptide comprising the sequence of the CDE,

(d) structurally stabilizing the peptide by circularization so that the CDE is present in its native conformation.

9. The method of claim 8, wherein the circularization of the peptide is achieved by generating cysteine bridges, bridging amino acid side chains that form a pseudopeptide.

10. The method of claim 8 or 9, wherein the peptide is generated using amino acids carrying glycosylation moieties which are present on the protein of interest.

11. The method of any one of the preceding claims 8 to 10, wherein it comprises the step:

(e) conjugating the peptide to a carrier molecule selected from haptens, polypeptides, peptides, and the protein of interest.

12. A peptide or polypeptide comprising a CDE, obtainable by the method of any one of claims 8 to 11.

13. Use of a peptide or polypeptide of any one of claims 1 to 7 as an immunogen for the generation of immunomodulatory substances specifically recognizing the CDE in its natural environment.

14. Use of a peptide or polypeptide of any one of claims 1 to 7 for the immunisation of animals or transgenic animals expressing human FcγRIIa or FcγRIIb.

15. Use of a peptide or polypeptide of any one of claims 1 to 7 for the generation of antibodies that can specifically recognize alleles of the

FcγRIIa Arg/His polymorphism at position 131 or the FcγRIIa Val/Phe polymorphism at position 155.

16. A method of producing substances capable of discriminating between an antigen of interest and closely related antigens, wherein the method comprises immunising an animal with a peptide or polypeptide according to any one of claims 1 to 7 or/and with a correctly folded peptide derived from FcγRIIb or FcγRIIa, and isolating the resulting antibodies, and optionally using the antibodies to generate recombinant immunomodulatory substances.

17. A substance characterized by the ability to specifically bind to the peptide or polypeptide of any one of claims 1 to 7.

18. An antibody or fragment or derivative thereof, wherein it specifically binds to human FcγRIIb or FcγRIIa in the natural environment of the Fc receptor.

19. The antibody of claim 18, wherein it binds with higher affinity to FcγRIIb than to FcγRIIa, preferably with at least 10fold, more preferably at least 100fold, more preferably at least 1,000fold, more preferably at least 10,000fold, more preferably at least 100,000fold, more preferably at least 1,000,000fold higher affinity to FcγRIIb than to FcγRIIa.

20. The antibody of claim 18, wherein it binds with higher affinity to FcγRIIa than to FcγRIIb, preferably with at least 10fold, more preferably at least 100fold, more preferably at least 1,000fold, more preferably at least 10,000fold, more preferably at least 100,000fold, more preferably at least 1,000,000fold higher affinity to FcγRIIa than to FcγRIIb.

21. The antibody or fragment or derivative thereof of claim 18, 19 or 20 wherein it is able to specifically block IgG binding to human FcγRIIb or

FcγRIIa.

22. The antibody or fragment or derivative thereof of any one of claims 18 to 21, wherein it does not interfere with immune complex binding to FcγRIIb or FcγRIIa.

23. The antibody or fragment or derivative thereof of claim 18, 19, 20 or 21, wherein it is capable of inhibiting the physiological function of human FcγRIIb or FcγRIIa.

24. The antibody or fragment or derivative thereof of claim 18, 19, 20 or 22, wherein it is capable of activating the physiological function of human FcγRIIb or FcγRIIa.

25. The antibody or fragment or derivative thereof of claim 18, 19, 20, 22 or claim 24, wherein it is able to specifically cross-link human FcγRIIb or FcγRIIa.

26. The antibody or fragment or derivative thereof of any one pf claims 18 to 25, wherein it occurs in a monomeric or multimeric state.

27. The antibody or fragment or derivative thereof of any one of claims 18 to 26, wherein it is capable of binding to a CDE of FcγRIIb or FcγRIIa.

28. The antibody or fragment or derivative thereof of claim 27, wherein it is capable of binding to an epitope of human FcγRIIb or FcγRIIa comprising at least one of amino acids 12, 27, 29, 30, 104, 127, 132, 135, 160 and 171 of the amino acid sequence of FcγRIIb or FcγRIIa according to SEQ ID NO: 1 or SEQ ID NO: 2.

29. The antibody or fragment or derivative thereof of claim 28, wherein it is capable of binding to an epitope of FcγRIIb or FcγRIIa comprising amino acids 27 to 30, and/or 127 to 135, and/or 160 to 171 of the amino acid sequence of FcγRIIb or FcγRIIa according to SEQ ID NO: 1 or SEQ ID NO: 2.

30. The antibody or fragment or derivative thereof of any one of claims 18 to 29, wherein it is a polypeptide carrying a complementarity determining region (CDR) which is specific for FcγRIIb.

31. The antibody or fragment or derivative thereof of claim 30, wherein it is a polypeptide carrying one or more of the CDR-sequences according to SEQ ID Nos: 5, 7, 9 and 11.

32. The antibody or fragment or derivative thereof of any one of claim 18 to 31, wherein it is of the class IgG, IgE, IgM or IgA.

33. The antibody or fragment or derivative thereof of any one of claims 18 to 32, wherein it is selected from single chain antibodies, bi-functional antibodies and tri-functional antibodies, Fab fragments, $F(ab)_2$ fragments, Fv fragments and scv-fragments.

34. An antibody or part hereof, according to any one of claims 18 to 33, characterised in comprising the variable light and/or heavy regions of antibody GB3 according to SEQ ID NO: 5 and 7, or a portion thereof having specificity; or the variable light and/or heavy regions of antibody CE5 according to SEQ ID NO: 9 and 11 or a portion thereof having specificity.

35. A nucleic acid sequence encoding the peptide of any one of claims 1 to 7 or the antibody or fragment or derivative thereof according to any one of the claims 18 to 34.

36. The nucleic acid of claim 35 encoding the sequence of monoclonal antibodies CE5 or GB3 according to SEQ ID NOs: 4, 6, 8 and 10 or a portion thereof.

37. A nucleic acid vector comprising the nucleic acid sequence according to claim 35 or 36.

38. A host cell transfected with a vector according to claim 37.

39. A pharmaceutical and/or diagnostic composition useful for the treatment and/or diagnosis of diseases associated with Fc receptor mediated signaling, in particular rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, Rieter's syndrome, psoriasis or lupus erythematosus, comprising an effective amount of the antibody, fragment or derivative thereof according to any one of claims 18 to 34, and pharmaceutically acceptable carrier substances.

40. A diagnostic kit for the detection of autoimmune diseases and/or cancer, comprising the antibody, fragment or derivative thereof according to any one of claims 18 to 34 and/or the recombinant peptide or polypeptide according to any one of claims 1 to 7.

41. Use of the antibody or fragment or derivative thereof of any one of claims 18 to 34 for the production of inhibitors or activators of the FcγRIIa/IgG interaction or the FcγRIIb/IgG interaction.

42. Use of the antibody or fragment or derivative thereof of any one of claims 18 to 34 for the production of a pharmaceutical and/or diagnostic composition for the diagnosis and/or treatment of autoimmune diseases, Systemic Lupus Erythematosus, Rheumatoid Arthritis, Immune Thrombocytopenic Purpura or Multiple Sclerosis.

43. Use of the antibody or fragment or derivative thereof of any one of claims 18 to 34 for the production of a pharmaceutical and/or

diagnostic composition for the diagnosis and/or treatment of cancer, in particular lymphomas or leukemias.

44. Use of the antibody or fragment or derivative thereof of any one of claims 18 to 34 as an adjuvant with other biotherapeutics for the treatment and/or diagnosis of cancer.

45. Use of claim 44, wherein the other therapeutics are selected from the group comprising the antibodies Herceptin®, Rituxan®, IC14, PANOREX™, IMC-225, VITAXIN™, Campath 1H/LDP-03, LYMPHOCIDE™ und ZEVLIN™, and antibodies binding to the following cancer antigens: MAGE-1, MAGE-3, BAGE, GAGE-1, GAGE-2, N-acetylglucosaminyltransferase, p15, beta-catenin, MUM-1, CDK-4, HER-2/neu, human papillomavirus E6, human papillomavirus-E7 and MUC-1.

46. Use of the antibody or fragment or derivative thereof of any one of claims 18 to 34 for the production of a pharmaceutical and/or diagnostic composition for the diagnosis and/or treatment of allergies.

47. Use of the antibody or fragment or derivative thereof of any of claims 18 to 34 for the production of a pharmaceutical and/or diagnostic composition for the treatment of diseases associated activated dendritc cells and/or macrophages.

48. Use of the antibody or fragment or derivative thereof of any of claims 18 to 34 for the production of a pharmaceutical and/or diagnostic composition for the treatment of host-versus-graft disease.

49. Use of the antibody or fragment or derivative thereof of any of claims 18 to 34 for the production of a pharmaceutical and/or diagnostic composition for the treatment of amyloid linked diseases.

50. Use of the antibody or fragment or derivative thereof of any of claims

18 to 34, wherein the antibody or fragment or derivative thereof comprises specific anti- FcγRIIa fragments in bi-specific antibodies to direct antigens towards transport by thrombocytes and/or uptake by the liver and spleen phagocytosis system.

51. Use of the antibody or fragment or derivative thereof of any of claims 18 to 34, wherein the antibody or fragment or derivative thereof is a specific anti-FcγRIIa antibody or fragment thereof for the production of a pharmaceutical and/or diagnostic composition for the diagnosis and/or treatment of ITP.

52. Use of the antibody or fragment or derivative thereof of any of claims 18 to 34 for the production of a pharmaceutical composition to increase the effect of vaccination.

53. Antibody or fragment or derivative thereof of any one of claims 18 to 34, wherein it is modified in the Fc-fragment by the modification of the glycosylation and/or mutagenesis to enhance the binding towards subsets of the Fc-receptors.